UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
YOSHIO JO, MOTONORI AOSHIMA, KOJI TANABE, KOICHI MATSUSHITA, and TOSHIKI INOUE

Appeal No. 2006-0647
Application No. 10/069,561
Technology Center 1600

ON BRIEF

Before SCHEINER, MILLS, and GRIMES, *Administrative Patent Judges.*

SCHEINER, *Administrative Patent Judge.*

DECISION ON APPEAL

Appellants appeal under 35 U.S.C. § 134 from the final rejection of claims 34, 36-55, 57-60, and 62-74, all the claims remaining, under 35 U.S.C. § 103. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

DISCUSSION

The present invention is directed to a "soluble trauma-healing hemostatic cellulose fiber containing coagulation protein[,]" which "readily dissolve[s] on contact with blood," and "exhibit[s] a hemostatic effect due to

stimulation of the agglutination reaction of fibrin monomer which is formed from fibrinogen by the action of [ ] thrombin present in the . . . fiber[,] and as a result of the stabilization of the agglutinates through a cross-linking reaction of [ ] coagulation factor XIII" (Specification 3: 15-26). The fiber also "promotes the adhesion and agglutination of [ ] platelets to the trauma locus due to the rapid dissolving thereof on contact with [ ] blood or body fluids present in the trauma site" (*id.* at 3: 33-36).

Claims 34 and 53 are representative of the subject matter on appeal and read as follows:

> 34. A soluble trauma-healing hemostatic cellulose fiber, comprising a natural or regenerated cellulose fiber that has been partially carboxymethylated to an extent such that degree of substitution of the hydroxyl groups in the glucose units constituting the cellulose molecule is 0.5 - less than 1.0,
>
> wherein three types of coagulation proteins being fibrinogen, thrombin and coagulation factor XIII are applied or chemically bonded to said fiber followed by drying,
>
> such that said fiber possesses activity for accelerating a coagulation reaction of fibrin monomers converted from fibrinogen with thrombin and possesses activity for stabilizing agglutinates by cross-linking reaction with the coagulation factor XIII.
>
> 53. A method of producing a soluble trauma-healing hemostatic cellulose fiber, comprising the steps of:
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> treating a natural or regenerated cellulose fiber with an aqueous sodium hydroxide solution,
>
> reacting the thus-treated fiber with a monochloro acetic acid solution for carboxymethylation to an extent such that degree of substitution of hydroxyl groups of the glucose units constituting the cellulose molecule (etherification degree) is 0.5 to less than 1.0,
>
> subsequently refining the fiber and then imparting or chemical bonding three coagulation proteins which are fibrinogen, thrombin and coagulation factor XIII, to the refined cellulose fiber, and

then drying the fiber,

whereby said fiber possesses activity for accelerating a coagulation reaction of fibrin monomers converted from fibrinogen with thrombin, and possesses activity for stabilizing the agglutinates by the cross-linking reaction with the coagulation factor XIII.

The Examiner relies on the following prior art:

Sugitachi	4,265,233	May 5, 1981
Colombo	4,340,731	Jul. 20, 1982
Edwardson	5,962,026	Oct. 5, 1999
Soe	EP 0 956 869 A2	Nov. 17, 1999

The Examiner rejected claims 34, 36-55, 57-60, and 62-74 as unpatentable over the combined teachings of Soe, Colombo, Edwardson, and Sugitachi. Again, the claims are directed to a soluble, partially carboxy-methylated cellulose fiber, and a method of making it, wherein the degree of substitution of the hydroxyl groups in the glucose units of the cellulose fiber is from 0.5 to less than 1.0, and wherein fibrinogen, thrombin, and factor XIII are applied or chemically bonded to the fiber.

"In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

> A rejection based on section 103 clearly must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, all facts must be considered. The Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because *it* may *doubt* that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual

> basis. To the extent the Patent Office rulings *are* so supported, there is no basis for resolving doubts against their correctness. Likewise, we may not resolve doubts in favor of the Patent Office determination when there are deficiencies in the record as to the necessary factual bases supporting its legal conclusion of obviousness.

In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967) (emphasis in original).

Soe describes "a tissue sealant which can seal injuries, reduce loss of blood, maintain a hemostasis, and promote healing of an injured site" (Soe 2: 7-9). The sealant is a liquid or powder (*id.* at 4: 41), prepared "by admixing thrombin and carboxylmethyl cellulose . . . with fibrinogen" (Soe 3: 32-33) and other proteins, including coagulation factor XIII (*id.* at 4: 49). "A carboxylmethyl cellulose which may be used . . . is etherified with carboxylmethyl groups at a part or all of [the] hydroxy groups" (*id.* at 3: 36-37). "The degree of etherification with carboxylmethyl groups . . . is preferably 0.5 to 1.5, more preferably 0.6 to 0.95, . . . to ensure an appropriate water-solubility" (*id.* at 3: 40-41). Soe does not describe fibers of any kind.

Colombo describes a method of producing a "carboxyalkyl-cellulose [fiber] that is practically hydroinsoluble, . . . and that possesses a high absorption and retention power or capacity, [ ] towards water[,] . . . saline solutions, . . . physiological and plasmatic liquids" (Columbo col. 1, ll. 44-49). Cellulose, "in the form of fibers . . . is dispersed in an organic diluent" (*id.* at col. 2, ll. 9-11), and "brought into contact with . . . sodium hydroxide, . . . so as to form the alkali-cellulose" (*id.* at col. 2, ll. 17-19). "The alkali-cellulose . . . is etherified by a treatment with . . . monochloroacetic acid"

and "[t]he degree of substitution . . . is such as to render the corresponding carboxyalkyl-cellulose soluble in water, . . . said degree of substitution is . . . between 0.4 and 1.5" (*id.* at col. 2, ll. 21-29). "After removal of the [organic] diluent, the carboxyalkyl-cellulose . . . is subjected to a heat-treatment . . . so as to achieve the internal cross-linking of the carboxyalkyl-cellulose, and thus make it practically insoluble in water" (*id.* at col. 2, ll. 62-68). Colombo's insoluble, absorbent "cellulosic products . . . are particularly suitable for use in sanitary towels or napkins, bandages, tampons, and the like" (*id.* at col. 6, l. 67 to col. 7, l. 2).

Edwardson describes a method of making non-crosslinked fibrin monomers or polymers by passing plasma over a thrombin-like enzyme immobilized on a solid support, which can be made from a number of materials, including cellulose (Edwardson col. 8, l. 67 to col. 9, l. 35).

Sugitachi describes "a wound healing material capable of effectively promoting the formation of stabilized fibrin at a wound site . . . for a long period of time" (Sugitachi col. 1, ll. 39-45). The wound healing material comprises a structure, wherein "[t]he term 'structure' . . . refers to all conventional materials used in healing a wound site, which may have various forms such as monofilaments; fibrous assemblies, such as cotton, paper, non-woven fabrics, woven fabrics, and knitted fabrics; films; sponges; etc." (*id.* at col. 1, ll. 49-55). "Examples of the materials which make up such structures [include] . . . [c]ellulose, viscose rayon, cupraammonium rayon, cellulose acetate, carboxymethyl cellulose, methyl cellulose," etc. (*id.* at col. 1, l. 64 to col. 2, l. 1).

According to the Examiner, both Soe and Sugitachi "deal with wound-treating compositions that may comprise carboxymethyl cellulose, thrombin, and Factor XIII" (Answer 6); Soe teaches that "low-substituted carboxymethylcellulose is preferred" (*id.* at 5); Colombo discloses "methods of producing low-substituted cellulose ether" (*id.*), and Edwardson teaches that "a thrombin-like enzyme may be immobilized . . . through various activation chemistries . . . [and] [s]uitable supports . . . include cellulose and cellulose derivatives" (*id.* at 4). Based on these teachings, the Examiner concluded that "[i]t would have been obvious to one of ordinary skill in the art . . . to combine the references of the prior art into the object of the rejected claims" (*id.* at 5).

Appellants argue that the present claims require "a *soluble*, trauma-healing hemostatic cellulose fiber containing (three types of) coagulation proteins [ ] which rapidly *dissolves* when contacting blood" (Brief 10), but Soe "*fails* to disclose a hemostatic *fiber*" (*id.* at 8), and the fibrous cellulose materials of Colombo and Sugitachi "are *not* designed for dissolution as claimed" (*id.*).

Appellants' point is well taken, especially as Colombo's focus is on producing "carboxyalkyl-cellulose that is practically hydroinsoluble" (Colombo col. 1, ll. 44-45), and Sugitachi's carboxymethyl cellulose structures appear to be insoluble as well, as they are intended to "promote the formation of stabilized fibrin at the wound site for long periods of time" (Sugitachi col. 8, ll. 60-61).

That being the case, we see no factual basis for the Examiner's assertion that "the collective disclosure of the prior art has shown the

instantly claimed . . . partially carboxymethylated cellulose having fibrinogen, thrombin, and coagulation factor XIII bonded onto it . . . , [and] it stands to reason that such cellulose material would exhibit the same attributes as claimed by the appellant, such as solubility and rapid dissolution" (Answer 9).

We agree with Appellants that the cited references, viewed without the benefit of hindsight, would not have suggested the claimed soluble hemostatic fiber, or the claimed method of making it, to a person of ordinary skill in the art. As discussed above, the Examiner may not "resort to . . . unfounded assumptions or hindsight reconstruction to supply deficiencies in [the] factual basis" of the rejection (*Warner*, 379 F.2d at 1017, 154 USPQ at 178).

We conclude that the examiner has not established a prima facie case of obviousness on this record, and we are constrained to reverse the rejection of claims 34, 36-55, 57-60, and 62-74 under 35 U.S.C. § 103(a) as unpatentable over Soe, Colombo, Edwardson, and Sugitachi.

OTHER ISSUES

As discussed above, none of the references cited by the Examiner describe soluble carboxymethyl cellulose fibers, with or without fibrinogen, thrombin, and factor XIII. According to the present specification, however, Japanese Patent Application No. Hei11-58412 describes "a soluble trauma-healing hemostatic cellulose fiber whose hydroxyl groups in the glucose units . . . of the natural or regenerated cellulose fibers have been partially carboxymethylated so that its carboxymethyl substitution level . . . becomes 0.5 - under 1.0%" (Specification 2: 32 to 3: 2). It is not clear from the

record whether the Examiner ever considered an English translation of this document, or whether it even qualifies as prior art. Upon return of this application to the Examiner, we would urge the Examiner to evaluate the relevance of this document to the patentability of the present invention, especially in light of Soe's teachings.

CONCLUSION

We conclude that the examiner has not established a prima facie case of obviousness and the rejection of claims 34, 36-55, 57-60, and 62-74 under 35 U.S.C. § 103(a) is reversed.

REVERSED

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